(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
4 January 2001 (04.01.2001)

PCT

(10) International Publication Number
WO 01/00849 A1

(51) International Patent Classification[7]: C12N 15/54, 9/10, C07K 16/40, C12Q 1/68, 1/48, A61K 38/45 // A61P 35/00

(21) International Application Number: PCT/US00/17827

(22) International Filing Date: 28 June 2000 (28.06.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/141,582 29 June 1999 (29.06.1999) US

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(81) Designated States *(national)*: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*
— *Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/00849 A1

(54) Title: TANKYRASE2 MATERIALS AND METHODS

(57) Abstract: The invention provides novel tankyrase polypeptides designated tankyrase2, polynucleotides encoding the polypeptides, expression constructs comprising the polynucleotides, and host cells transformed with the expression constructs. Also provided are methods for producing the tankyrase2 polypeptides, antibodies that are immunoreactive with the tankyrase2 polypeptides. In addition, there are provided methods for identifying specific binding partners of tankyrase2, and more particularly methods for identifying binding partners that modulate biological activity of tankyrase2. Methods of modulating biological activity of tankyrase2 *in vitro* and *in vivo* are also provided.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/17827

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/54 C12N9/10 C07K16/40 C12Q1/68 C12Q1/48
A61K38/45 //A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
BIOSIS, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 15647 A (GARVAN INST MED RES ;SUTHERLAND ROBERT LYNDSAY (AU); DALY ROGER JO) 1 April 1999 (1999-04-01) page 8 -page 10, line 24 page 13 -page 17 ---	7
A	SMITH S ET AL: "Tankyrase, a poly(ADP-ribose) polymerase at human telomeres" SCIENCE, vol. 282, no. 5393, 20 November 1998 (1998-11-20), pages 1484-1487, XP002118903 ISSN: 0036-8075 cited in the application --- -/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 December 2000	11/12/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Andres, S

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/17827

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 00 61813 A (FUNK WALTER D ;MORIN GREGG B (US); GERON CORP (US); PIATYSZEK MIEC) 19 October 2000 (2000-10-19) page 2, line 9 -page 3, line 15 examples claims figure 4 -----	1,3,4, 6-17, 19-26

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/17827

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9915647 A	01-04-1999	AU 9245898 A	12-04-1999
		EP 1017802 A	12-07-2000
WO 0061813 A	19-10-2000	NONE	

WHAT IS CLAIMED IS:

1. A purified and isolated tankyrase2 polypeptide.

2. The polypeptide according to Claim 1, comprising the amino acid sequence defined in SEQ ID NO:133.

3. The polypeptide according to Claim 1, comprising the amino acid sequence defined in SEQ ID NO:135.

4. A polynucleotide encoding the polypeptide according to Claim 1.

5. The polynucleotide according to Claim 4, comprising the coding region of the nucleotide sequence defined in SEQ ID NO:132.

6. The polynucleotide according to Claim 4, comprising the coding region of the nucleotide sequence defined in SEQ ID NO:134.

7. A polynucleotide selected from the group consisting of:

(a) the polynucleotide according to Claim 4,

(b) a polynucleotide complementary to the polynucleotide of (a), and

(c) a polynucleotide that hybridizes under moderately stringent hybridization conditions to the polynucleotide of (a) or (b).

8. The polynucleotide according to Claim 7, wherein the polynucleotide is a DNA molecule or an RNA molecule.

9. The polynucleotide according to Claim 8, further comprising a detectable label moiety.

10. An expression construct, comprising the polynucleotide according to Claim 4.

11. A host cell transformed or transfected with the expression construct according to Claim 10.

12. The polynucleotide according to Claim 4, wherein the polynucleotide is operatively linked to a heterologous promoter.

13. A host cell, comprising the polynucleotide according to Claim 12.

14. A method for producing a tankyrase2 polypeptide, comprising the steps of:

a) growing the host cell according to Claim 11 or 13 under conditions appropriate for expression of the polypeptide; and

b) isolating the polypeptide from the host cell or the medium in which the host cell is grown.

15. An antibody that is specifically immunoreactive with the polypeptide according to Claim 1.

16. The antibody according to Claim 15, wherein the antibody is selected from the group consisting of monoclonal antibodies, polyclonal antibodies, single chain antibodies (scFv antibodies), chimeric antibodies, bifunctional/bispecific antibodies, humanized antibodies, human antibodies, CDR-grafted antibodies, Fab fragments, Fab' fragments, $F(ab')_2$ fragments, and Fv fragments.

17. A cell line that produces an antibody according to Claim 15.

18. An anti-idiotype antibody that is specifically immunoreactive with an antibody according to Claim 15.

19. A method for identifying a binding partner of a tankyrase2 polypeptide, comprising:

a) contacting the tankyrase2 polypeptide with a test compound under conditions that permit binding of the tankyrase2 polypeptide and the test compound;

b) detecting binding of the test compound and the tankyrase2 polypeptide; and

c) identifying the test compound as a binding partner of the tankyrase2 polypeptide.

20. The method according to Claim 19, wherein said specific binding partner selectively or specifically modulates a biological activity of the tankyrase2 polypeptide.

21. A method for identifying a specific binding partner of a tankyrase2 polynucleotide, comprising:

a) contacting the tankyrase2 polynucleotide with a test compound under conditions that permit binding of the tankyrase2 polynucleotide and the test compound;

b) detecting binding of the test compound and the tankyrase2 polynucleotide; and

c) identifying the test compound as a specific binding partner of the tankyrase2 polynucleotide.

22. The method according to Claim 21, wherein said binding partner selectively or specifically modulates activity of the tankyrase2 polynucleotide.

23. A method of treating an animal having a medical condition mediated by poly(ADP-ribose) polymerase activity, comprising administering to said animal a tankyrase2 inhibitory compound in an amount effective for inhibiting tankyrase2 activity in said animal.

24. The method according to Claim 23, wherein said medical condition is associated with growth of neoplastic tissue.

25. The method according to Claim 24, wherein said neoplastic tissue is a cancer selected from the group consisting of carcinomas, sarcomas, leukemias, and lymphomas.

26. The method according to Claim 25, wherein said cancer is selected from the group consisting of ACTH-producing tumor, acute lymphocytic leukemia, acute nonlymphocytic leukemia, cancer of the adrenal cortex, bladder cancer, brain cancer, breast cancer, cervical cancer, chronic lymphocytic leukemia, chronic myelocytic leukemia, colorectal cancer, cutaneous T-cell lymphoma, endometrial cancer, esophageal cancer, Ewing's sarcoma, gallbladder cancer, hairy cell leukemia, head and neck cancer, Hodgkin's lymphoma, Kaposi's sarcoma, kidney cancer, liver cancer, lung cancer (small and non-small cell), malignant peritoneal effusion, malignant pleural effusion, melanoma, mesothelioma, multiple myeloma, neuroblastoma, glioma, non-Hodgkin's lymphoma, osteosarcoma, ovarian cancer, ovarian (germ cell) cancer, pancreatic cancer, penile cancer, prostate cancer, retinoblastoma, skin cancer, soft tissue sarcoma, squamous cell carcinomas, stomach cancer, testicular cancer, thyroid cancer, trophoblastic neoplasms, uterine cancer, vaginal cancer, cancer of the vulva, and Wilm's tumor.